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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR   | ATTORNEY DOCKET NO.  | CONFIRMATION NO. |
|-----------------|-------------|------------------------|----------------------|------------------|
| 09/865,048      | 05/24/2001  | Leon W.M.M. Terstappen | 890-2FWC/CIP/CPA/CON | 2293             |

23869 7590 09/09/2003

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| EXAMINER |
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YAEN, CHRISTOPHER H

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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1642

DATE MAILED: 09/09/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/865,048

**Applicant(s)**

TERSTAPPEN ET AL.

**Examiner**

Christopher H Yaen

**Art Unit**

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 9-11, 13-16 and 19-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9-11, 13-16 and 19-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. The amendment filed 5/30/2003 (paper no. 13) is acknowledged and entered into the record. Accordingly, claims 12,17-18, and 30-52 are canceled without prejudice or disclaimer.
2. Claims 9-11, 13-16, and 19-29 are therefore pending and examined on the merits.

### **NEW ARGUMENTS**

#### ***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 9,10,11,13,15,16,19-26,28, and 29 are rejected under 35 U.S.C. 102(a) as being anticipated by Tse TW *et al* (WO 94/26787).

a. Claims are drawn to method of obtaining phage particles comprising antibody fragments directed against antigens associated with the surface of a target cell wherein the target cells are in a heterogeneous population of cells of which are detectably labeled, comprising the steps of: (i) providing a library expressing phage particles that express antibody fragments, (ii) incubating said library with heterogeneous population of cells, (iii) separating the target cells bound with phage particle from the non-target cells, and (iv) recovering the phage particles (claim 9). The claims are further limited to the separation of the

target cells and phage particles by flow cytometry (claim 10); cells labeled with a fluorescent label (claim 13); repeating steps (ii-iv) (claim 15); and the phage particles express Fab or scFv (claim 16). The claims are also drawn to a method of obtaining phage particles comprising an antibody fragment directed against the surface of a target cell comprising the steps of: (i) providing a library expressing phage particles that express antibody fragments, (ii) incubating said library with non-target cells, (iii) incubating library with target cells, (iv) separating the target cells bound with phage particle from the non-target cells, and (v) recovering the phage particles (claim 19). The claims are further limited to immobilized non-target antigen (claim 20); non-target antigens are coated onto a solid support (claim 21); non-target antigens associated with the cell surface of a non-target cell (claim 22); separation of target cells and phage particles by flow cytometry (claim 23); isolating the antibody fragments that bind to the target cell (claim 24); the target cells and or non-target cells are detectably labeled (claim 25), wherein the detectable label is a fluorescent label (claim 26); repeating steps (ii-v) (claim 28); and the phage particles expressing Fab or scFv (claim 29).

b. Tse TW *et al* disclose a method of generating monoclonal antibodies against unpurified antigens associated with the surface of a cell. Tse TW *et al* teach the steps of incubating phage antibody library with a mixed cell population (see page 3, paragraph 1); separating the target cells with the bound phage particles, wherein the method can be accomplished by FACS (see page 5, lines 22-28 and example 2); and recovering the bound phage particle from the target

cell (see abstract figure). Tse TW *et al* further indicate that the repeating of the steps several times would phage particles with high specificity (see page 4, lines 20-22), and that the antibodies generated from the enrichment process can be in the form of Fabs (see page 9, lines 24-25). It is also disclosed that the cells act as solid supports and thus claims that read on the non-target antigens bound to solid supports are also anticipated (see page 2, lines 23-24). Furthermore, FACS or fluorescent activated cell sorting is a process that inherently requires the cells being "sorted" to be detectably labeled, in any event, TSE TW *et al* teach of detectably labeling target cells for separation (see page 9, example 2).

***Claim Rejections - 35 USC § 103***

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 19-11, 13-16, and 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tse TW *et al* (cited above) in view of Verwer *et al* (EP 0610774A1). Claims 9-11, 13, 15-16, 19-26, and 28-29 are discussed above, claims 14, and 27 are drawn to specific fluorescent labels fluorescein (claim 14) and PE, PerCP, and FITC (claim 27). Tse TW *et al* teach a method of isolating phage particles directed against cell surface antigens, however, Tse TW *et al* do not specifically teach the fluorochromes listed in claims 14 and 27.

This deficiency is made up by Verwer *et al*, wherein Verwer *et al* disclose a method of flow cytometry involving cells labeled with FITC or PE (see abstract)

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It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to label the target and/or non-target cells with fluorochromes such as FITC or PE, given the teachings of Verwer *et al*, in order to practice the methods of Tse TW *et al* for the separation of cells using a flow cytometry technique. Moreover, one of ordinary skill in the art would have been motivated to use any fluorochrome label as taught by Verwer *et al* due to the fact that the labels are functionally equivalent in that they are covalently attached to a cell expressing an antigen and provided a fluorescent signal that would be detected by a flow cytometry cell sorter.

### ***Double Patenting***

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 9-11, 13-16, and 19-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S.

Patent No. 6,265,150 (previously cited and herein referred to as '150) in view of Tse

TW *et al*. See above for discussion of claims. It would have been *prima facie* obvious

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at the time the invention was made to one of ordinary skill in the art to obtain phage particles directed against a cell surface antigen using a heterogeneous cell population as a antigen source that was labeled with a fluorochrome because both the '150 patent taught a method of obtaining the phage particles. However, the '150 patent does not specifically teach the addition of non-target cells prior to the addition of target cells. This deficiency is made up by Tse TW *et al* because Tse TW *et al* disclose that non-target cells can be pre-incubated with the phage particles prior to the addition of the target cells (see example 2). One of skill in the art would had found motivation to combine the two references because both disclose methods of isolating or obtaining phage particles that have specificity to cell surface antigens. One of skill could have expected a reasonable amount of success in pre-incubating the non-target cells with phage particles prior to the addition of target cells because Tse TW *et al* disclosed that non-specific binding of the phage particles could be diminished.

**All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in Paper No. 13.**

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*Christopher Yaen*  
for:

Christopher Yaen  
Art Unit 1642  
September 4, 2003